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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/763,559	06/04/2001	Brian Allen Moser	342312001600	7874

7590 01/27/2004

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/763,559	MOSER ET AL.	
	Examiner	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, IDS AND STATUS OF THE CLAIMS

1. The amendment, remarks, and the information disclosure statement (IDS) and Form PTO-1449 filed 10/20/03 are acknowledged, entered and considered. In view of Applicant's request claims 1, 4, 7, 8, 12-14, 18 and 20 have been amended. Thus, claims 1-22 are now pending in the application. The objection of the abstract and the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 1023(a) over the prior art are withdrawn in view of Applicant's amendment and remarks filed 10/20/03. Applicant's amendment, arguments with respect to the rejections under 35 U.S.C. 102(b) and 103(a) over the prior art of record have been considered but deemed to be moot in view of the new ground of rejection necessitated by Applicant's amendment.

NEW GROUND OF REJECTION

2. **CLAIMS REJECTION-35 U.S.C. § 103(a)**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions

covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/47645 taken with Boeck et al. (The Journal of Antibiotics, Vol. XLII, No. 3, pp. 382-388, 1989), Jamison et al., (The Journal of Antibiotics, Vol. 51, No. 2, pp. 239-242, 1998) and Balkovec et al., (U.S. Patent No. 5,378,804).

WO 97/47645 discloses on page 6, compound III and in reaction scheme I and II, a reversible cyclic peptide adduct (aza cyclohexapeptide) an Echinocandin comprising a boric or boronic acid complexed with a cyclic peptide having 1,2-cis-diol, and the boronic acid is selected from the group consisting of alkyboronic acid or phenylboronic acid. Thus, meeting the limitation of claims 1-3. The patent discloses a similar structure of Echinocandin as claimed in claim 4 because Echinocandin is defined on page 7 in the instant specification to refer to compounds having the general structure recited in claim 4 including any simple derivatives thereof (See compound III and claim 1 of '645 patent). On reaction scheme I and II and Example 1, the prior art clearly discloses a method for forming a reversible cyclic peptide adduct by using an aqueous borane complex solution by adding a cyclic peptide compound having 1,2-cis-diol moiety to said aqueous solution by reacting a free acid with a suitable organic or inorganic base, or alternatively by reacting a free base with a suitable organic or inorganic acid and thereby adjusting the pH to a value sufficient to effect complexation

between the boric acid and cyclic peptide, and as such, resulting in higher yields and easier synthesis of the analogs of the compounds. Thus, meeting the limitations of claims 7-10. Further, on page 26, first paragraph the prior art discloses the adjustment of pH of the aqueous solution, in which the pH was adjusted until the solution of the filtrate was greater than pH 5, and as such meets the limitation of claim 11. On pages 4-5, the reference discloses a pharmaceutical formulation comprising a complex of a boric or boronic acid with a cyclic peptide having a 1,2-ics-diol moiety with acceptable carrier thereof, and as such meet the limitations of claims 14-18.

The primary reference of WO 97/47645 differs from claims 1-22 in not teaching a) the use of cyclic peptide adduct which is more water soluble than the parent peptide from which the adduct is derived, b) the use of a reversible cyclic peptide (Echinocandin) adduct having the structure of aminophenyl group and the structure recited in claim 6, c) method of purifying a cyclic Echinocandin peptide thereof, and d) method for treating a fungal infection by administering the pharmaceutical formulation comprising the compound of claim 4 thereof. The primary reference of WO 97/47645 discloses cyclohexapeptide compounds (including Echinocandin) and a method for forming a reversible cyclic peptide adduct, comprising adding a 1,2-cis-diol cyclic peptide to an aqueous solution of a boric or boronic acid by adjusting the pH of the solution to a value sufficient for complexation and a pharmaceutical formulation thereof. It is also known in the art that borate and boronate adducts are ionic in character, the hydrophilicity or water-solubility of the complexed material is enhanced as acknowledged by Applicant on pages 5 and 6 in the instant specification. Thus, materials containing a 1,2-cis-diol moiety that are generally insoluble or only slightly soluble in aqueous solutions can be made more soluble or more soluble in aqueous solutions by forming a borate or boronate adduct (i.e., use of borate and boronate

makes the complexed material more water soluble than the parent from which it is formed). Further, the secondary reference of Boeck et al. reports the Echinocandin B (ECB) deacylation techniques, however, on page 387, the reference states that while studying the effects of various buffering agents, ECB was found to be soluble in 10^{-2} M borate under slightly alkaline conditions. Addition of borate to the complexed material likewise resulted in almost total solubilization of the ECB. Thus, clearly showing the use of borate to enhance the hydrophlicity of water-solubility of the complexed material.

Furthermore, the secondary reference of Jamison et al., discloses on Figure 1, the use of a reversible cyclic peptide adduct based on ECB having the structure of aminophenyl group. On pages 240-241, the reference discloses the isolation, purification and *in vitro* and *in vivo* testing of the product for antifungal activity comprising adding a 1,2-cis-diol cyclic peptide to an aqueous solution by adjusting the pH of the solution at about 7 pH to a value sufficient for complexation of the cyclic peptide adduct. Moreover, the secondary reference of Balkovec et al., discloses aza cyclohexapeptide compounds, e.g., Echinocandins used as antifungal agents to treat fungal infections such as myotic infections in mammals, especially those caused by *Candida* species such as *C. albicans*, *C. tropicalis*, etc. Thus, clearly showing the administration of the compound for the treatment of fungal infections (See e.g., col. 3, lines 29-46). Also, the reference discloses the purification of the cyclic peptide using substantially the same method steps as claimed in claims 12 and 13 and the formulation of pharmaceutical composition thereof (See e.g., col. 7, lines 18 to col. 8, lines 42; and col. 13, lines 35 to col. 14, lines 45).

Thus, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the primary reference's teachings of cyclohexapeptide compounds (such as Echinocandins) and a method for forming a

reversible cyclic peptide adduct, comprising adding a 1,2-cis-diol cyclic peptide to an aqueous solution of a boric or boronic acid by adjusting the pH of the solution to a value sufficient for complexation and a pharmaceutical formulation thereof into the secondary references of Boeck et al. teachings which shows that the addition of borate to the complexed material resulted in almost total solubilization of the ECB and Jamison et al. complexes of 1,2-cis-diol cyclic peptide adduct having the structure of aminophenyl group and their use as a means for purification, isolation, stabilization and/or water solubilization, wherein the compounds result in increasing their water solubility, and of Balkovec et al., aza cyclohexapeptide compounds useful for as antifungal agent to treat fungal infections such as myotic infections in mammals.

Therefore, the combined teachings of the prior art makes obvious the use of a reversible borate or boronate complexes of 1,2-cis-diol cyclic peptide which may include Echinocandin adduct which is more soluble than the parent peptide from which the adduct is derived, method for forming the boronate adduct, method of purifying reversible adduct, pharmaceutical formulation of reversible adduct and method for treating infections thereof, absent of sufficient objective factual evidence or unexpected results to the contrary.

CLAIMS REJECTION-35 U.S.C. § 112 [1st] PARAGRAPH

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which

it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6, 8 and 18-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4, 8 and 18 as amended on 10/23/03 contain new matter because the original specification does not appear to support "**R^7 is-CH_3**". The specification on pages 3 and 7 discloses structures with R^7; however, there is no recitation that "**R^7 is-CH_3**". Thus, claims 4, 8 and18 and claims depending thereof have no support for the "**R^7 is-CH_3**" from the original disclosure because there is no disclosure in the specification as now claimed. Thus, Applicant respectfully requested to either cancel all unsupported subject matter or to show where such subject matter has support from the original disclosure

OBJECTION TO THE ABSTRACT OF THE DISCLOSURE

LANGUAGE

4. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology

often used in patent claims, such as "means" and "said," should be avoided. Also, the use of the phrase "for example or e.g.," should be avoided because it is unclear whether the limitation(s) following the phrase is/are part of the disclosed invention. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

5. **ACTION IS FINAL, NECESSITATED BY AMENDMENT**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272-0955. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

AAM Mohamed/AAM

January 20, 2004

Christopher S. F. Low

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
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